PULSED ULTRASOUND AS A CONTROLLED, DYNAMIC MECHANICAL FORCE INPUT

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Mechanical deformation has been demonstrated to regulate phenotypic expression of cells involving various signal transductive pathways. However, application of mechanical input to tissue structures in vivo is not easily achieveable. To this end, low intensity ultrasound (US) has been employed as a methodology for noninvasive application of a controlled mechanical force input. This technique has been shown to have a significant effect on the rate of fracture repair in animal models and bone repair in humans. The mechanisms proposed for the US response include both direct mechanical effects due to matrix or membrane deformation or indirect due to localized fluid flow. The objective of these studies has been to characterize the biochemical response to applied US in order to optimize physical models of the input signal.

MC3T3-E1, MC3T3-E1/J1 and TE-85 osteoblastic cells were used in these studies. The US exposure system consisted of an array of four-2.5 cm PZT-4 transducers specifically designed for a four well tissue culture plate (Nunc). This array is at the bottom of a water tank and the culture plate is located at the transition of the far field region. Unidirectional propagation of the US signal perpendicular to the cell monolayer is accomplished using an absorption chamber on top of the culture plate which was coupled directly to the culture media through thin film domes minimizing standing wave generation. The US signal consisted of a 200 /sec burst of 1.5 MHz sine waves repeating at 1 kHz, with power outputs ranging from .5 to 75 mW/cm.^{2}. (SATA). All experiments were performed at 37 C in a humidified incubator. Adenylate cyclase was measured using 3H-adenine by the Salomon method. TGF-beta synthesis was determined using the mink lung epithelial cell bioassay.

US exposure of MC3T3 and TE85 osteoblasts decreases the adenylate cyclase response at 5 and 15 minutes by 45 and 40% respectively, and inhibits the PTH response by up to 80% at 15 minutes. TGF-beta biosynthesis is inhibited by short term US stimulation at 2-6 hours post-exposure, in contrast to hormonal activation (PTH), which increased TGF-beta levels. These results suggest that US induces a mechanical input which affects the adenylate cyclase transductive pathway. The ability of the US to decrease the PTH response indicates that the effect of US on adenylate cyclase may be receptor mediated. Future work will continue to develop the association between mechanical sensitivty and US signal parameters.